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Daniel Pratt

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EXAMINER

ALSTRUM ACEVEDO, JAMES HENRY

ART UNIT

PAPER NUMBER

1616

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/723,626	Applicant(s) PRATT ET AL.	
	Examiner JAMES H. ALSTRUM ACEVEDO	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 January 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22-31 and 39-52 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22-31, 39-44 and 48-52 is/are rejected.
- 7) ☒ Claim(s) 45-47 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Claims 22-31 and 39-52 are pending. Applicants previously cancelled claim 1-3, 4-21, and 32-38. Claims 42-52 are new. Receipt and consideration of Applicants' amended claim set and remarks/arguments submitted on January 30, 2009 are acknowledged. All rejections not explicitly maintained in the instant office action have been withdrawn per Applicants' claim amendments. Applicants' claim amendments have necessitated new grounds of rejection set forth below (e.g. rejections under §112, 2nd paragraph)

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 51 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (new matter). The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants' new claim 51 indicates that the buoyancy agent and the therapeutic agent are the same, and have indicated that support for this limitation can be found at page 18, line 11 and page 30, line 13. The cited locations in Applicants' specification refer to a list of possible therapeutic agents and buoyancy agents, respectively, wherein both lists recite Vitamin E. A search of Applicants' specification did not uncover any statements supporting the general notion that the therapeutic agent and buoyancy agent present in the composition

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administered in the claimed method may be the same. The cited alleged support is not considered to support the concept that any possible therapeutic agent contemplated by Applicants' specification may simultaneously be both the buoyancy agent and the therapeutic agent required to be present in the composition administered by Applicants' claimed method. Thus, claim 51 is considered to constitute new matter, whereas claim 52 does not contain new matter, because Vitamin E is clearly identified by Applicants' specification as being both a suitable buoyancy agent as well as a suitable therapeutic agent. If Applicants believe that support exists for the limitation of claim 51 in other parts of their specification, they are kindly requested to cite specific page and line numbers where support may be found.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 42-43 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 42-43 are vague and indefinite because these claims claim a range of specific gravity of "greater than about 1.0063" and "less than about 1.0063," respectively. The term "about" is not defined by Applicants' specification. An ordinary skilled artisan would be unable to ascertain the metes and bounds of the recited specific gravity ranges because the minimum or maximum endpoint cannot be unambiguously determined. As a result the ordinary skilled artisan would be forced to guess at the possible meaning intended by the term about as well as what was the actual specific gravity range required by claims 42-43.

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Claim 49 recites the limitation "a liquid" in line 2. There is insufficient antecedent basis for this limitation in the claim. Parent claim 22 indicates that the buoyancy agent may be a gas, oil, or combination thereof. Thus, reference in dependent claim 49 to the buoyancy agent being selected from a gas, a liquid, or combination thereof lacks antecedent basis, because a liquid is broader in scope than reference to an oil.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

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the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 22-30, 40-44, and 48-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soon-Shiong et al. (U.S. Patent No. 5,560,933) ("Soon-Shiong").

Applicant Claims

Applicants claim (1) a method of administering a therapeutic agent within the central nervous system (CNS) comprising intrathecal administration of a composition to a subject's CNS, wherein said composition comprises a biodegradable polymer having a therapeutic agent and a buoyancy agent contained therein, wherein the buoyancy agent is selected from gases and oils and is controllably buoyant within the CSF.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Soon-Shiong teaches methods for in-vivo delivery (e.g. intrathecal administration) of substantially water insoluble pharmacologically active agents (e.g. taxol) and compositions useful thereof (title; abstract; col. 3, lines 24-29; and col. 4, lines 28-33). Soon-Shiong's invented compositions comprise particles of substantially water insoluble active agents contained within a shell having a cross-sectional diameter of no greater than 10 microns, wherein a cross-sectional diameter of less than 1 micron is most preferred (col. 5, lines 23-30). Suitable active agents for incorporation into Soon-Shiong's invented compositions include aspirin, ibuprofen, estrogen (i.e. a hormone), prednisolone, cortisone, hydrocortisone, anesthetics,

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immunosuppressive agents, and preferably **taxol (i.e. a cytotoxic agent)** (col. 5, lines 31-56).

The invented composition may also contain nutritional agents within the shell, such as **amino acids**, sugars, **proteins, carbohydrates, fat-soluble vitamins, such as vitamins A,D, E, and K**, and combinations thereof (col. 5, line 65 through col. 6, line 3). **Amino acids, sugars, proteins, carbohydrates, and vitamins A, E, and K read on active agents that are “other plant products”**. The shell of Soon-Shiong's invented particles can be made of any natural or synthetic biocompatible polymer that may be cross-linked via the formation of disulfide linkages, such as **proteins** (e.g. **albumin, insulin, hemoglobin, immunoglobulins, fibronectin, fibrinogen**, etc.), **oligopeptides, polysaccharides** (e.g. starch, cellulose, chitin, dextrans, etc.), and synthetic polymers, which are amenable to chemical functionalization to introduce sulfhydryl moieties, such as polyvinyl alcohol, **polyhydroxyethyl methacrylate**, polyacrylic acid, polyacrylamide, polyvinyl pyrrolidone, etc.

Soon-Shiong teaches that optionally in the preparation of the compositions dispersing agents in which the active agent is dissolved or suspended may also be included, such as **vegetable oils (e.g. soybean oil, coconut oil, olive oil safflower oil, cotton seed oil, and the like)**, aliphatic, cycloaliphatic, or aromatic hydrocarbons having 4-30 carbon atoms, aliphatic or aromatic alcohols, esters, ethers, and alkyl or aryl halides, all having 2-30 carbon atoms are indicated as being suitable dispersing agents (col. 6, lines 47 through col. 7, line 4). The invented particles with a biocompatible shell and an active agent contained therein are typically **delivered as a suspension in a biocompatible aqueous liquid** (col. 7, lines 15-22). In the preparation of Soon-Shiong's invented compositions, it is contemplated that **the particle shells contain therein both the substantially water insoluble active agent dissolved or suspended**

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in the dispersing agent (col. 8, line 65 through col. 9, line 7). In Example 2 (col. 11, lines 12-35), Soon-Shiong teaches **an albumin protein shell containing soybean oil**. Shells comprising **a mixture of albumin and PEG-thiol** with a molecular weight of 2,000 g/mol are also exemplified in Example 11, col. 16, lines 20-55). The inclusion of PEG is art-recognized as increasing protein/enzyme in vivo circulation time and is expected to prolong drug release in vivo (col. 9, lines 38)

***Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)***

Soon-Shiong does not exemplify a method of administering a therapeutic agent by intrathecal administration. This method, however, is suggested per the teachings of Soon-Shiong. Soon-Shiong does not explicitly teach the inclusion of buoyancy agents. This deficiency is nonetheless obvious per Soon-Shiong's teachings.

***Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)***

It would have been prima facie obvious at the time of Applicants' invention to utilize the invented particles to administer an active pharmaceutical agent intrathecally, because Soon-Shiong explicitly teaches that the invented compositions are suitable for the in vivo administration of active substances and defines in vivo delivery to include intrathecal administration. Soon-Shiong does not explicitly teach the inclusion of buoyancy agents, however, Soon-Shiong's invented particles may comprise a dispersing agent, such as vegetable oils, which Applicants' admit are suitable buoyancy agents. Thus, Soon-Shiong's teachings

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suggest the administration of biocompatible aqueous suspensions of particles comprising (i) a biocompatible shell, such as cross-linked albumin, which is also biodegradable, and (ii) a substantially water insoluble active agent dissolved or suspended in a dispersing agent, such as soybean oil, which is necessarily a buoyancy agent, as admitted by Applicants. An ordinary skilled artisan would have been motivated to administer Soon-Shiong's compositions intrathecally and would have had a reasonable expectation of success in intrathecally administering these compositions, because Soon-Shiong's compositions are taught as being suitable for intrathecal administration. Regarding the intrathecal administration of Soon-Shiong's compositions to patients diagnosed with a central nervous system disorder, the preferred active agent in Soon-Shiong's compositions is a taxol, which is a well-known anticancer agent.

It is noted that "cancer" reads on a central nervous system disorder, as evidenced by Applicants' claim 28. Anti-cancer agents, such as taxol, read on the term "neuroprotective agent" as defined by Applicants in paragraph [0024] (i.e. "neuroprotective agent" refers to drugs which alleviate a symptom of or prevent damage to the brain or spinal cord"), because an anti-cancer agent would prevent further damage to the brain or spinal cord caused by cancer as well as treat symptoms caused by the cancer.

Regarding the recited specific gravity ranges, Applicants have identified vegetable oils as having a specific gravity that is less than 1.0063. Because the term about has not been defined, it is the Examiner's position that a specific gravity of "about 1.0063", regardless of whether the recited specific gravity is indicated as being greater than or less than, would necessarily include values above and below 1.0063. Thus, vegetable oil would necessarily have a specific gravity of

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“about 1.0063.” Regarding the incorporation of PEG (polyethylene glycol), it would have been *prima facie* obvious to include PEG. Regarding claims 51-52, because Soon-Shiong teaches that the particles may contain fat-soluble vitamins as the active ingredient (e.g. Vitamin E), most of these vitamins are oils, and that the dispersing agent may be removed, Soon-Shiong’s teachings impliedly suggest biodegradable particles containing an oil that would act as both a buoyancy agent and a therapeutic agent when administered to the CSF. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Response to Arguments

Applicant's arguments filed 1/30/2009 have been fully considered but they are not persuasive. Applicants’ traverse the instant rejection by arguing (1) intrathecal administration is mentioned in a “laundry list” in Soon-Shiong, (2) “Soon-Shiong” does not recite the term “buoyancy agent” or specifically make reference to composition components as providing buoyancy, (3) the particles disclosed by Soon-Shiong are allegedly unsuitable, because the polymeric shells would biodegrade to release the active agent, thus the compositions would lose the benefit of the buoyancy agent, (4) Soon-Shiong utilizes oils for a different stated purpose than Applicants, (5) Soon-Shiong’s compositions would require “substantial” modification to be suitable for intrathecal administration, (6) the term "suspend" is contemplated by Applicants to mean suspension in the CSF, whereas the term "suspend" is contemplated by Soon-Shiong to

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mean suspension of the active in the dispersing agent, and (7) the rejection is based upon improper hindsight.

The Examiner respectfully disagrees with Applicants' traversal arguments. Regarding (1) and (7), Applicants' characterization of Soon-Shiong's list of 11 specific suitable routes of administration as a "laundry list" is mistaken. A list of 11 specific components is not a "laundry list" by any stretch of the imagination, because the list is sufficiently small to permit each individual member to be clearly envisaged. Selection of intrathecal administration from among the 11 specific routes of administration indicated by Soon-Shiong as being suitable is not cherry picking, and also does not constitute improper hindsight. Furthermore, in response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Regarding (2), Applicants' are correct that Soon-Shiong's teachings do not include the term "buoyancy agent," however, this observation overlooks the fact that Soon-Shiong explicitly discloses and exemplifies polymeric particles for the intrathecal administration of an active agent containing a vegetable oil within said particles. See Example 2: col. 11, lines 11-35. Applicants have identified vegetable oil as being a buoyancy agent. The fact that Soon-Shiong does not use the term "buoyancy agent" does not change the fact that particles containing a buoyancy agent (i.e. vegetable oil) are explicitly exemplified by Soon-Shiong. Thus, Soon-Shiong does in fact

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suggest the intrathecal administration of particles comprising a therapeutic agent and a buoyancy agent.

Regarding (3), if Soon-Shiong's particles are no less suitable than the particles disclosed by Applicants' as comprising biodegradable polymers (e.g. Applicants' claims 22 and 30). Thus, the characterization of Soon-Shiong's particles as being unsuitable for intrathecal administration is disingenuous, especially wherein Applicants also claim the intrathecal administration of biodegradable polymers containing a buoyancy agent.

Regarding (4), the prior art is not required to recite the same motivation that induced Applicants' to develop their claimed invention. Rather the prior art is merely required to provide *a* motivation for obtaining biodegradable particles containing a buoyancy agent (e.g. vegetable oil, such as soya oil) and a therapeutic agent and to administer these particles intrathecally. The teachings of the prior art provide ample motivation to obtain such particles and clearly suggest intrathecal administration. Thus, the prior art provides ample motivation that does not rely upon impermissible hindsight reasoning.

Regarding (5), it is unclear what Applicants mean by the term "substantial modification." This argument is interpreted to suggest that Soon-Shiong's teachings do not enable intrathecal administration. This is found unpersuasive, because Soon-Shiong explicitly indicates that the invented particles are suitable for intrathecal administration. Attorney argument in the absence of objective evidence that Soon-Shiong's particles cannot be administered intrathecally is unpersuasive. Furthermore, the fact that an ordinary skilled artisan might require some experimentation to delivery Soon-Shiong's invented particles intrathecally does not establish that Soon-Shiong's particles cannot be administered absent undue experimentation.

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Regarding (6), Soon-Shiong's compositions would necessarily be suspended in the CSF as contemplated by Applicants' wherein these particles contain entrapped dispersing agent, such as soya oil, etc. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention. The instant rejection is maintained.

Claims 31 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soon-Shiong et al. (U.S. Patent No. 5,560,933) ("Soon-Shiong") as applied to claims 22-30, 40-44, and 48-52 above, and further in view of Russell et al. (*Bone Marrow Transplantation*, 1999, 24, pp 1177-1183) (already of record) and Vook et al. (US 2003/0129233).

Applicant Claims

Applicants claim method as described above, wherein the biodegradable polymer is poly(lactide-co-glycolide) (PLGA) and in some embodiments the active agent consists of living cells selected from bone marrow cells (e.g. red blood cells), fetal neural cells, or stem cells.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Soon-Shiong have been set forth above in the instant office action and are herein incorporated by reference. The teachings of Russell were set forth in the office action mailed 6/2/06 and are restated herein. Russell is provided herein to demonstrate that living cells, specifically bone marrow stem cells and blood cell stem cells, are art recognized therapeutic

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agents used in the treatment of leukemia. Leukemia is a kind of cancer and living cells are clearly substantially water insoluble active agents.

Russell teaches comparative studies of the treatment of patients with acute myelogenous leukemia (AML) and Myelodysplasia (MDS) who received sibling transplants with stem cells from peripheral blood (blood cell transplant, BCT) or bone marrow (BMT). Russell concluded by stating that while disease-free survival may be better using BCT than BMT for AML, it may greatly impair quality of life, due to a higher proportion of acute graft-versus-host disease (GVHD) (abstract).

Vook teaches particularly effective compositions for the localized delivery of chemotherapeutic hydrophobic anticancer agents, inclusive of paclitaxel (taxol), doxorubicin, 5-fluorouracil, camptothecin, cisplatin, and metronidazole, their corresponding derivatives and functionally equivalents, and combinations thereof from PLGA microspheres [0006]. Vook's invented PLGA/Taxol microspheres afford controlled/sustained release of taxol and offer many clinical advantages, such as (1) improved patient compliance, as the number of drug dosings are decreased because the depot contains an amount of drug equivalent to multiple doses; (2) isolation depot from the tissue via its incorporation in PLGA thus reducing the drug concentration exposed to the one time and decreasing the chance of tissue injury of the drug copolymer, tissue at any at the depot site; (3) controlled drug release, which may allow for increased dosages of hydrophobic drugs to be administered without systemic toxicity complications. In terms of specific clinical applications of this technology, hydrophobic drug/PLGA formulations are envisioned to play a role in the treatment regiment of cancer and of infection [0287].

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***Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)***

Soon-Shiong lacks the teaching of an intrathecal administration method, wherein the active agent consists of living cells. This deficiency is cured by the teachings of Russell. Soon-Shiong lacks the teaching of an intrathecal administration method, wherein the biodegradable polymer is PLGA. This deficiency is cured by the teachings of Vook.

***Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)***

It would have been prima facie obvious to modify the teachings of Soon-Shiong to substitute taxol for bone marrow stem cells or red blood stem cells, because both bone marrow stem cells or red blood stem cells have been shown as being suitable for treating leukemia a kind of cancer and taxol is a known anti-cancer agent. Furthermore, it would have been prima facie obvious to substitute taxol for bone marrow stem cells or red blood stem cells to treat leukemia, a kind of cancer, because both taxol and bone marrow stem cells or red blood stem cells are known to be suitable for the treatment of cancer. An ordinary skilled artisan would have been motivated to utilize bone marrow stem cells or red blood stem cells as the active agent in Soon-Shiong's invented compositions, because bone marrow stem cells or red blood stem cells are clearly substantially water insoluble active agents. An ordinary skilled artisan would have had a reasonable expectation of success upon incorporation of bone marrow stem cells or red blood stem cells into Soon-Shiong's invented compositions, because bone marrow stem cells or red blood stem cells are substantially water insoluble active agents. Regarding the use of PLGA as the biodegradable polymer shell, this would have been prima facie obvious, because PLGA is a

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well-known conventional biocompatible and biodegradable polymer. An ordinary skilled artisan would have been motivated to modify Soon-Shiong's teachings and utilize PLGA/taxol microspheres, because PLGA/taxol microspheres are conventional compositions used to deliver taxol, are reasonable expected to enhance patient compliance due to the controlled/sustained release properties of the PLGA/taxol microspheres, and taxol is isolated from the body in the PLGA microsphere and, thus, less likely to induce tissue damage. An ordinary skilled artisan would have had a reasonable expectation of modifying Soon-Shiong's teachings to utilize PLGA as the polymer shell and obtain suspensions wherein the polymer shells contained taxol suspended in a dispersing agent (e.g. vegetable oil) and deliver the resulting composition intrathecally, because Soon-Shiong's compositions are suitable for intrathecal administration and taxol/PLGA are well known compositions. Thus, an ordinary skilled artisan would have been motivated to utilize Soon-Shiong's invented composition modified to contain bone marrow or red blood stem cells in to treat cancer via intrathecal administration with a reasonable expectation of success.

Response to Arguments

Applicant's arguments filed 1/30/2009 have been fully considered but they are not persuasive. Applicants' traverse the instant rejection is based upon the same arguments rebutted above in with regards to the first rejection under § 103(a). The Office's rebuttal is herein incorporated by reference. The instant rejection is maintained.

Allowable Subject Matter

Claims 45-47 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The art of record does not suggest the preparation of biodegradable polymer particles containing therein a therapeutic agent in combination with (i) a mixture of oxygen and nitrogen, (ii) a hydrofluorocarbon, or (iii) a gas selected from the group consisting of oxygen, nitrogen, argon, carbon dioxide, helium, and xenon, and combinations thereof.

Conclusion

Claims 22-31, 39-44, and 48-52 are rejected. Claims 45-47 are objected. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner is on a flexible schedule, but can normally be reached on M-F ~10am~5:30 pm, and Saturdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

J.H.A.-A.
Patent Examiner
Technology Center 1600

/Johann R. Richter/
Supervisory Patent Examiner, Art Unit 1616